REMARKS

In the claims

Claims 1–5 and 8–10 are currently under examination with claims 6–7 withdrawn from consideration due to restriction/election. Claims 11–16 are added by this paper.

Claim Amendments

New claims 11–16 recite additional aspects of the invention and are supported by throughout the instant specification, as originally filed. For example, the Office is courteously requested to refer to FIGS. 1–11 and the disclosure contained at pages 7–10 of the instant specification.

Rejection under 35 U.S.C. § 103(a)

The rejection of the claims under 35 U.S.C. § 103(a) as allegedly being unpatentable over Hiraishi et al. in view of Mountfort et al. is respectfully traversed.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation...to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference must teach or suggest all the claim limitations. See MPEP §2143.

Hiraishi describes a bovine liver phosphoamidase which can hydrolyze (N–P) bonds of N-phosphorylated compounds. See, col. 1, lines 1–3 of the introduction at page 368 of Hiraishi et al. Hiraishi further discloses that the 13 kDa phosphoamidase hydrolyzes N-phosphorylated amino acids but not N-phosphorylated substrates such as phosphocreatine or O-phosphorylated substrates such as glucose-6-phosphate and phosphotyrosine. See the DISCUSSION section at page 372 of the cited reference. Hiraishi does not teach or suggest the use of any of the substrates claimed herein. See, Applicants' claim 1.

The Office Action then proceeds to allege that Hiraishi's deficiencies can be compensated by Mountfort's disclosure of fluorometric substrates such as FDP. However, Mountfort's assay technique is drawn to the detection of hydrolysis of phosphate

monoester (P–O) bonds in the phosphor-ester metabolizing phosphatase, PP-2A. See, pages 911–912 of Mountfort et al. The Examiner is also courteously requested to review Section 10.3, part 2 of the reference by Molecular Probes for background information on protein phosphatases. Mountfort does not teach or suggest the use of FDP substrate for the assessment of phosphoamidase activity.

Applicants courteously submit that a combination of Hiraishi and Mountfort, even at their broadest scope, would not lead one of ordinary skill in the art to reformulate the prior art to arrive at what is claimed by the instant application. Mountfort only uses FDP for detecting the activity of a phosphatase. Neither reference fully encompasses the enzyme-substrate combination of the Applicants' claimed method. As such, even if one were to combine all the reference teachings, there would be no way, absent hindsight, to arrive at the claimed methods. Furthermore, nothing would lead a skilled worker to use Mountfort's substrates to assay Hiraishi's phosphoamidase activity, given the fact that Hiraishi's disclosure clearly indicates that its bovine phosphoamidase is not able to hydrolyze O–P bonds of glucose-6-phosphate and Mountfort discusses only hydrolysis of O-P bonds. Therefore, it is respectfully submitted that the cited references, either solely or in combination, would fail to render obvious what is claimed by the instant application. As such, the rejection under 35 U.S.C. §103(b) must be withdrawn.

Hiraishi's brief mention of possible use of glucose-6-phosphate and phosvitin as potential substrates of phosphoamidase does not change the conclusion, at least because neither of these particular two substrates is the same as or analogous to the five recited substrates of the claims. This Hiraishi sentence does not motivate a skilled worker to employ any of the five recited substrates at all, let alone with a reasonable expectation of success.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 1–5 and 8–10 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly being non-enabled. Applicants courteously traverse this rejection.

At page 3, the Office Action alleges that the specification "does not reasonably provide enablement for the detection of *all phosphoamidases* and/or the hydrolysis of a

phosphor-ester bond of at least one of the substrates." Applicants respectfully disagree with this contention. It is submitted that the specification, coupled with a skilled worker's knowledge, provides adequate guidance on how to use the claimed compounds. "To be enabling, the specification of the patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation." Genentech Inc. v. Novo Nordisk A/S, 108 F.3d 1361, 1365 (Fed. Cir. 1997) (quoting *In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir. 1993)). For example, the instant specification and the references cited therein provide description of the term "protein phosphoamidase" and the activity of such enzymes against "phosphoamide (P-N) bonds of phosphorylated basic amino acids." See, *e.g.*, page 3, lines 13–34 of the instant specification. In particular, the specification provides numerous representative examples on methods for assaying for the activity of such proteins using the claimed set of five substrates. See, *e.g.*, FIGS. 6–8 and the description of the figures provided at pages 7–8 of the specification. Moreover, the specification utilizes a variety of control setups to support the claimed methods and provides detailed guidance on various operative and inoperative embodiments. The specification provides description on the operability of the claimed method under various reaction conditions and phases. For example, FIG. 1 provides information on pH dependency of the reaction; FIG. 2 provides information on the kinetics of the reaction; FIG. 11 provides guidance on conducting a gel-based assay. In short, the instant specification is fully commensurate with what is claimed by the Applicants' invention.

Applicants courteously submit that the Office's reliance on Hiraishi's disclosure is grossly misplaced. At the outset, it is submitted that Hiraishi's observation is derived from the ability of bovine liver phosphoamidase to hydrolyze glucose-6-phosphate or phosphotyrosine. See, the discussion section of Hiraishi et al. These specific compounds are not the subject matter of the instant invention, and more importantly, Hiraishi does nothing to demonstrate that the claimed assay would not work with the instantly claimed substrates. Therefore, the allegation that "certain phosphoamidases are able to hydrolyze nitrogen-phosphorus (N–P) bonds as well as oxygen phosphorus (O–P) bonds, while certain phosphoamidases only hydrolyze N–P bonds and certain phosphoamidases only hydrolyze phosphorylated arginine," says nothing about the nature of the instant specification. Even if such were true, the standard for enablement is whether a skilled

person could determine whether certain embodiments that were conceived, but not yet made, would be inoperative or operative using routine procedures. Atlas Powder Co. v. E.I. du Pont de Nemours & Co., 750 F.2d 1569, 1577, 224 USPQ 409, 414 (Fed. Cir. 1984); MPEP 2164.08(b). The specification provides clear guidance on how to test for candidate proteins that fall within the scope of the claims. Testing for the desired functional activity would constitute routine experimentation, which, given the state of the art and the detailed disclosure of the Applicants' instant specification, can be performed both reliably and reproducibly by one of ordinary skill in the art. In fact, if the Office is correct in interpreting Hiraishi, this contributes to enablement in that a skilled worker could then even more routinely omit testing the known phosphoamidases which are inappropriate.

The Office's contention that undue experimentation would be required to arrive at the majority of the proteins of the claimed genus is also untrue in view of Applicants' detailed disclosure. For example, Applicants have utilized control setups to objectively test the claimed subject matter. Moreover, it is courteously submitted that the Office has not presented any evidence to reasonably doubt the objective truth of the claims. The courts have placed the burden upon the PTO to provide evidence shedding doubt on the disclosure that the invention can be made and used as stated; see, e.g., *In re Marzocchi*, 439 F.2d 220, 169 U.S.P.Q. 367 (CCPA 1971) (holding that how an enablement teaching is set forth, either by use of illustrative examples or by broad terminology, is of no importance.) The disclosure must be taken as in compliance with the enablement requirement of the first paragraph of Section 112, first paragraph unless there is reason to doubt the objective truth of the statements contained therein. See *Marzocchi*, supra. No such evidence or reason for doubting Applicants' disclosure has been provided. Only speculative statements and conclusions are made.

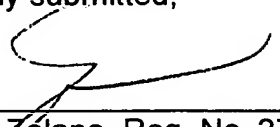
In view of the above remarks, it is respectfully submitted that applicants' disclosure provides more than sufficient guidance to objectively enable one of ordinary skill in the art to make and use the claimed invention with an effort that is routine with in the art. Withdrawal of the rejection under 35 U.S.C. §112, first paragraph, is respectfully requested.

In view of the above remarks, favorable reconsideration is courteously requested. If

there are any remaining issues which could be expedited by a telephone conference, the Examiner is courteously invited to telephone counsel at the number indicated below.

No fees are believed to be due with this response; however, the Commissioner is hereby authorized to charge any fees associated with this response to Deposit Account No. 13-3402.

Respectfully submitted,



Anthony J. Zelano, Reg. No. 27,969
Attorney for Applicant(s)

MILLEN, WHITE, ZELANO
& BRANIGAN, P.C.
Arlington Courthouse Plaza 1, Suite 1400
2200 Clarendon Boulevard
Arlington, Virginia 22201
Telephone: (703) 243-6333
Facsimile: (703) 243-6410

Attorney Docket No.: **MERCK-2907**

Date: October 30, 2006